NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

JANSSEN PHARMACEUTICALS, INC. et al.,	
Plaintiffs,	Civil Action No. 08-5103 (SRC)
v.	**OPINION**
WATSON LABORATORIES, INC. et al.	
Defendants.	

CHESLER, U.S.D.J.

INTRODUCTION

Plaintiffs Janssen Pharmaceuticals, Inc. and Johnson & Johnson Pharmaceutical Research & Development, LLC (collectively, "Janssen") bring this action for patent infringement against Defendants Lupin Pharmaceuticals, Inc. and Lupin Limited (collectively, "Lupin"). Plaintiffs complain that, by filing Abbreviated New Drug Application ("ANDA") No. 200541 with the United States Food and Drug Administration, and by submitting a Paragraph IV certification asserting that U.S. Patent No. 6,214,815 (the "'815 patent") is anticipated, obvious, and invalid, Defendants have infringed the '815 patent, which Plaintiffs own. A bench trial on Lupin's patent invalidity defenses to infringement was held for 6 days, beginning on May 29, 2012, and ending on June 5, 2012, with closing arguments heard on August 14, 2012. Upon hearing the evidence presented at trial, this Court finds that Defendants have not proven that claims 1 and 4 of the '815 patent are invalid, and Judgment will be entered accordingly.

BACKGROUND

On February 17, 2010, in Civil Action No. 10-322, since consolidated into the instant case, this Court entered a consent Order in which the parties stipulated that the filing of Lupin's ANDA No. 200541 constitutes an act of infringement of claims l and 4 of the '8l5 patent under 35 U.S.C. § 271(c)(2), and that Plaintiffs should be granted partial summary judgment on the issue of infringement of claims 1 and 4 of the '8l5 patent, subject to Lupin's affirmative defenses of patent invalidity. It is these affirmative defenses that were the subject of this trial.

For convenience, this Opinion sometimes uses the phrase, "the '8l5 patent," to refer to the claims at issue, claims 1 and 4 of the '8l5 patent. This Opinion makes use of the following abbreviations: 1) ORTHO TRI-CYCLEN® LO is abbreviated as "OTCLO;" 2) ORTHO TRI-CYCLEN® is abbreviated as "OTC;" 3) micrograms is "mcgs" or "µg;" 4) ethinyl estradiol is "EE;" 5) oral contraceptive is abbreviated as "OC;" and 6) "skilled artisan" is shorthand for "a person of ordinary skill in the pertinent art."

STIPULATED FACTS

The parties stipulated to the following facts in the Final Pretrial Order ("FPO"):

> This case involves the combination oral contraceptive ORTHO TRI-CYCLEN® LO, which is sold by Plaintiff Janssen Pharmaceuticals, Inc. ORTHO TRI-CYCLEN® LO contains two active ingredients, the estrogen ethinyl estradiol and the progestin norgestimate. In the ORTHO TRI-CYCLEN® LO regimen, combinations of ethinyl estradiol and norgestimate are administered for 21 consecutive days, followed by 7 days without the administration of steroids. The estrogen dosage is kept constant at a daily dosage of 25 micrograms ("µg") - which is 0.025 milligrams ("mg") - per day for each of the 21 active pill-taking days, while the norgestimate dosage increases in a step-wise fashion every 7 days during the 21-day active pill-taking period (i.e., .180 mg for days 1-7, .215 mg for days 8-14, and .250 mg for days 15-21).
>
> The ORTHO TRI-CYCLEN® LO regimen is covered by claims 1 and 4 of U.S.

Patent No. 6,214,815 ("the '815 patent"). Claim 1 is a claim to a method of contraception comprising administering ORTHO TRI-CYCLEN® LO, while claim 4 is to a triphasic oral contraceptive unit.

Claim 1 of the '815 patent claims as follows:

A method of contraception which comprises administering for 21 successive days to a female of childbearing age a combination of 17α-ethinylestradiol and norgestimate for the first 7 days in a daily dosage corresponding to 25 μg of 17α-ethinylestradiol and 0.180 mg of norgestimate, for the succeeding 7 days a daily dosage equal to 25 μg of 17α-ethinylestradiol a[n]d 0.215 mg of norgestimate; and for the next 7 days a daily dosage equal to 25 μg of 17α-ethinylestradiol and 0.250 mg of norgestimate; followed by 7 days without estrogen and progestogen administration.

Claim 4 of the '815 patent claims as follows:

A triphasic oral contraceptive unit having 21 separate dosage units, adapted for successive daily oral administration comprising: 7 dosage units containing in admixture with a pharmaceutically acceptable carrier, 25 μg of 17α-ethinylestradiol and 0.180 mg of norgestimate, 7 dosage units containing in admixture with a pharmaceutically acceptable carrier, 25 μg of 17α-ethinylestradiol and 0.215 mg of norgestimate; and 7 dosage units containing in admixture with a pharmaceutically acceptable carrier, 25 μg of 17α-ethinylestradiol and 0.250 mg of norgestimate; and optionally containing 7 additional dosage units free of estrogen and progestogen.

ORTHO TRI-CYCLEN® LO has been on sale in the United States since October 2002. Janssen filed the provisional patent application which ultimately led to the '815 patent on December 23, 1998, and filed the non-provisional application which led to this patent on June 9, 1999. The '815 patent issued on April 10, 2001. The '815 patent is due to expire in 2019.

. . .

Prior to selling ORTHO TRI-CYCLEN® LO and filing for and obtaining the '815 patent, Janssen sold an oral contraceptive product known as ORTHO TRI-CYCLEN®, and continues to sell ORTHO TRI-CYCLEN® today. The chemical composition of ORTHO TRI-CYCLEN® LO is identical to ORTHO TRI-CYCLEN® with the exception of the daily dosage of estrogen during the 21 active pill-taking days. Both products utilize the same dosages of norgestimate in the same triphasic 7/7/7 regimen. ORTHO TRI-CYCLEN® LO contains 25 micrograms of ethinyl estradiol per day while ORTHO TRI-CYCLEN® contains

> 35 micrograms of ethinyl estradiol per day.
>
> In the mid-1980s, Janssen obtained several patents covering triphasic oral contraceptive regimens, including: U.S. Patent No. 4,616,006 (the "'006 patent"), U.S. Patent No. 4,628,051 (the "'051 patent"), U.S. Patent No. 4,544,554 (the "'554 patent"), and U.S. Patent No. 4,530,839 (the "'839 patent") (collectively, "the Pasquale patents"). The Pasquale Patents were of record during the prosecution of the '815 patent.
> . . .
>
> Watson and Lupin each stipulated that its ANDA filing constitutes an act of infringement of claims 1 and 4 of the '815 patent, pursuant to 35 U.S.C. § 271(e)(2). On June 24, 2009, the Court signed a stipulated order granting Janssen partial summary judgment against Watson on the issue of infringement of claims 1 and 4. (Dkt No. 43.) On February 17, 2010, the Court signed a stipulated order granting Janssen partial summary judgment against Lupin on the issue of infringement of claims 1 and 4. (Dkt No. 14 in Case No. 10-0322.) On January 25, 2011, the Court granted Janssen partial summary judgment that claims 1 and 4 of the '815 patent satisfy the utility requirement under 35 U.S.C. § 101, and the enablement requirement under 35 U.S.C. § 112. (Dkt No. 169.)

(FPO at 3-7.)

THE ISSUES FOR TRIAL

1. Have Defendants proven by clear and convincing evidence that claims 1 and 4 of the '815 patent are invalid as anticipated, pursuant to 35 U.S.C. § 102?

2. Have Defendants proven by clear and convincing evidence that claims 1 and 4 of the '815 patent are invalid as obvious, pursuant to 35 U.S.C. § 103?

3. Have Defendants proven by clear and convincing evidence that claims 1 and 4 of the '815 patent are invalid under the doctrine of non-statutory double patenting?

THE EVIDENCE AT TRIAL

What follows is selected excerpts from the testimony of the witnesses appearing in court at trial:

A. Testimony of Sarah Berga

Dr. Berga was qualified as an expert witness. Dr. Berga stated that claims 1 and 4, covering OTCLO, are obvious in view of OTC, as disclosed in the '554 and '006 patents. (5/29/2012 Tr. 82:17-21.) "[A]t the time of the '815 patent, the combined oral contraceptive market was transitioning to products that were lower than 30 to 35 mcgs of EE." (Id. at 83:6-8.) On questioning, Dr. Berga stated:

> Q. And is there any difference in effect on a woman who takes Ortho Tri-Cyclen Lo from a woman who takes Ortho Tri-Cyclen or any dosing regimen within the scope of the Pasquale patents?
>
> A. To illustrate that point, I'd like to illustrate Berga 34 slide, which shows that the difference really is a drop in the ethinyl estradiol level from 35 to 25, but the effect on the ovary is the same, so, there is the same suppression of follicular and egg development, and there's the same amount of stimulation in the endometrium with the same amount of withdrawal bleeding. In essence, it's the same.

(Id. at 90:9-20.) Dr. Berga stated that a 1996 article by Elstein stated that "there has been a trend for the development and marketing of low-dose estrogen-containing products at 20 mcgs." (Id. at 92:25-93:2.) Prior to the critical date, other researchers had taken existing an contraceptive regimen, Femodene, and modified it to reduce the EE dosage by 10 µg, resulting in Femodette. (Id. at 97:11-25.) Researchers similarly modified Marvelon to result in Mercilon. (Id. at 99:7-14.) "Cycle control was known to be good with 20 mcg products." (Id. at 103:3-4.) A study showed that Femodene and Femodette both exhibited good cycle control. (Id. at 103:21-23.) A

study of Marvelon and Mercilon found no negative effect on cycle control from the 10 µg reduction in EE dosage. (Id. at 104:2-5.)

Dr. Berga quoted from a 1997 journal article, which stated: "The bottom line is that you can lower the estrogen dose quite far and keep cycle control." (Id. at 105:1-3.)

On cross-examination, Dr. Berga was questioned about her consulting work for the pharmaceutical company Parke-Davis on the products Loestrin and Estrostep. Loestrin was an oral contraceptive product which used a 20 µg EE dosage and had, among some in the field, a reputation for poor cycle control. (5/30/12 Tr. 181:16-182:25.) Parke-Davis wanted to improve its cycle control, and the result was the product Estrostep, introduced in 1998, in which the total EE dosage was increased. (Id. at 182:6-183:7.)

In an article regarding the product Mircette, published in 1998, Dr. Berga wrote that the Mircette regimen was a modification of the Mercilon regimen, with increased EE dosage, which was intended to improve cycle control, among other reasons. (Id. at 210:23-211:4, 213:18-24.)

There is no clinically meaningful difference in cycle control between Ortho Tri-Cyclen and Ortho Tri-Cyclen Lo. (Id. at 223:14-23.) Dr. Berga stated that it was "probably correct" to say that skilled artisans would agree that the reduction in EE dosage that was the sole difference between OTC and OTCLO did not result in a substantial loss of cycle control. (Id. at 226:6-9.)

B. Testimony of Kurt Barnhart

Dr. Barnhart was qualified as an expert witness. Dr. Barnhart stated that there were progestin-only OCs on the market, but they have problems because "the estrogen helps control the bleeding." (5/31/2012 Tr. 261:19-24.) In the art, as of the critical date, there was "a general understanding that was accepted that cycle control is loosely associated with estrogen dose." (Id.

at 273:12-14.) When asked if the skilled artisan would have thought that reducing the estrogen dosage would have increased the likelihood of breakthrough bleeding and spotting, Dr. Barnhart said, "That' s what we may expect, and there's a lot of literature that says it's true. There's lots of literature that said we didn't find what we expected." (Id. at 319:13-15.) Dr. Barnhart agreed that he had written the following statement in an article: "Combination oral contraceptives containing 20 mcgs EE may be theoretically safer, this has not been proven and low dose estrogen COCs have higher rates of bleeding pattern disturbances." (Id. at 371:1-6.)

C. Testimony of Lee Shulman

Dr. Shulman was qualified as an expert witness. Dr. Shulman stated: "The '006 patent describes a very broad genus of hundreds of millions of potential regimens and not a limited class." (5/31/2012 Tr. 493:20-22.) He estimated that the genus disclosed "841,223,040 potential regimens." (Id. at 506:25.) He agreed that it was true that, both in 1998 and today, the only OC product on the market that has subinhibitory amounts of progestin and an ultra-low dose of estrogen is OTCLO. (Id. at 540:7-11.)

D. Testimony of Philip Darney

Dr. Darney was qualified as an expert witness. Dr. Darney stated:

> A person of ordinary skill in the art wouldn't have started with the Pasquale patents or Tri-Cyclen in developing an ultra-low-dose pill. If such a person nevertheless chose to base a pill on those patents, he or she would have made other changes to compensate for the effects of lowering estrogen. Without these changes, such a person would not have had a reasonable expectation of success, meaning either efficacy or cycle control. But unexpectedly, Ortho Tri-Cyclen Lo did have cycle control comparable to that of Ortho Tri-Cyclen.

(6/1/2012 Tr. at 619:20-620:6.)

Dr. Darney wrote an article, titled "OC Practice Guidelines Minimizing Side Effects,"

published in 1987, which said, "The frequency of breakthrough bleeding and spotting has been shown to increase as the estrogen dose decreases." (Id. at 629:18-22, 630:14-15.) He characterized this statement as a "ubiquitous observation." (Id. at 631:18.) A skilled artisan in 1998, reading the article by Kaunitz (Ex. PTX 163), would have understood that article to assert that "[i]f you go below 30 to 35 mcgs, your patients are likely to have higher rates of breakthrough bleeding and spotting." (Id. at 631:3-632:7.) Similarly, such an artisan would have also understood that article to teach that "[i]f you use a birth control pill with less estrogen, you'll have more bleeding." (Id. at 632:8-14.) As to this latter statement, Dr. Darney said: "It's in every textbook and every review article like this one about combined oral contraceptives." (Id. at 632:15-22.)

Dr. Darney stated that, because the Pasquale patents expressly prefer a 35 μg EE dosage, they would not serve as a starting point for the skilled artisan seeking to create a combination OC with a lower estrogen dosage. (Id. at 667:19-668:4.) Every example in the Pasquale patents uses a 35 μg EE dosage. (Id. at 668:5-6.) The '006 patent states that the purpose of the invention was to reduce total monthly steroid dose, but it also speaks of "a greater emphasis on a reduction of the progestogen dosage in oral contraceptives." (Id. at 669:21-25, 672:9-11.) The application for the '006 patent was filed in 1985, a time in which there was strong interest in reducing progestogen dosage in OCs. (Id. at 673:8-12.) Dr. Darney cited Exhibit PTX 192 as a journal article written by Pasquale, the named inventor on the Pasquale patents, published in 1986, which emphasized the importance of reducing progestogen dosage in a new generation of oral contraceptives while maintaining an acceptable bleeding pattern. (Id. at 673:20-674:10.)

A skilled artisan would not have had a reasonable expectation of success in taking the

OTC regimen and only reducing the EE dosage by 10 µg. (Id. at 729:16-20.) The skilled artisan, at the critical date, having read the Akerlund and Endrikat studies, would have thought that such a change would produce a substantial loss of cycle control. (Id. at 730:9-15.)

In 1996, when Dr. Darney co-authored an article giving OC prescribing guidelines (Exhibit PTX 181), he did not make a general recommendation for the use of regimens with EE dosages below 30 µg because of concerns about the associated irregular bleeding. (Id. at 776:15-21.) Instead, such regimens were recommended only for women with a particular sensitivity to estrogen. (Id. at 777:1-8.)

E. Testimony of Pierre Cremieux

Dr. Cremieux was qualified as an expert witness in the field of statistics. Dr. Cremieux stated that "there was no substantial statistical difference in cycle control between Ortho Tri-Cyclen and Ortho Tri-Cyclen Lo." (6/4/2012 Tr. 847:1-3.) He stated that the K90 "study was not sized to detect differences in cycle control." (Id. at 874:14-15.)

F. Testimony of Harry Boghigian

Mr. Boghigian was qualified as an expert in pharmaceutical marketing. Mr. Boghigian stated that marketing and promotion were "driving" the sales of OTCLO. (6/5/2012 Tr. 972:22-25.)

DISCUSSION

A. Patent invalidity: anticipation

Lupin contends that the '815 patent is invalid as anticipated by the '006 and '554 patents. There is no dispute that these patents teach the same regimen with only one difference material to this dispute: the only material difference between the contraceptive regimen disclosed in the

'006 and '554 patents and the one claimed in claims 1 and 4 of the '815 patent is that the prior patents disclose an EE dosage range of .02 - .05 mg, while claims 1 and 4 of the '815 patent require an EE dosage of .025 mg.[1] Lupin argues that, due to the range in the '006 patent, it constitutes a genus, within which the regimen at issue is one species, and that the genus anticipates the species.

The Federal Circuit has held:

> It is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus. *See, e.g., In re Baird*, 16 F.3d 380, 382 (Fed. Cir. 1994). There may be many species encompassed within a genus that are not disclosed by a mere disclosure of the genus. On the other hand, a very small genus can be a disclosure of each species within the genus.

Atofina v. Great Lakes Chem. Corp., 441 F.3d 991, 999 (Fed. Cir. 2006). The parties do not dispute that the relevant legal test used to determine whether a genus anticipates a species asks whether the prior art "expressly spelled out a definite and limited class of compounds that enabled a person of ordinary skill in the art to at once envisage each member of this limited class." Eli Lilly & Co. v. Zenith Goldline Pharms., Inc., 471 F.3d 1369, 1376 (Fed. Cir. 2006).

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[1] In particular, Defendants point to Example 4 and claim 9 of the '006 patent, which disclose the same regimen used in OTC. The specification of the '006 patent describes the invention as using an EE dosage in the range .02 - .05 mg, equivalent to a range of 20 to 50 µg. '006 patent col.2 ll.1-14. In the '554 patent, Defendants point to Example 4 and claim 10, which disclose the same regimen used in OTC. The specification of the '554 patent describes the invention as using an EE dosage in the range .02 - .05 mg, equivalent to a range of 20 to 50 µg. '554 patent col.2 ll.1-12.

Defendants generally focused their final briefing on the prior art '006 patent but, at times, point also to the '554 patent. Neither party has pointed to any material distinction between the '554 patent and the '006 patent. For convenience, this Opinion generally references only the '006 patent, as the parties have, but as neither party has meaningfully distinguished the two patents, the reasoning herein should be understood to apply to the '554 patent as well.

Defendants' argument has two major problems. The first is that it rests on a predicate which conflicts with the principle stated by the Federal Circuit in Lilly. Defendants argue that the class of possible regimens is limited to seven, because the skilled artisan would know to break the EE range of 20 to 50 micrograms into dosages evenly divisible by 5. Lilly, however, requires that the reference expressly spell out a definite and limited class. Defendants have not asserted that the '006 patent says anything about EE dosages being evenly divisible by 5. From the outset, then, Defendants have a problem: their argument rests not on a definite and limited class expressly spelled out in the '006 patent, but on a class they have constructed that is derived from the class stated in the reference. This would appear to imply that the '006 patent does not expressly spell out a definite and limited class, if Defendants must transform the stated EE range into something different. In this discussion, this Court uses the term "narrowing" to refer to the step in which Defendants transform the genus of regimens within the EE range of 20 to 50 micrograms into a set limited to only seven species. Defendants' "narrowing" approach fails for multiple reasons.

First, Defendants have offered no persuasive justification in Federal Circuit law for their efforts to "narrow." In making their anticipation case, Defendants rely on a key unsupported proposition: if a prior art reference discloses a genus containing a large number of species, a challenger may reduce the size of the genus by asking which species would have "stood out" to the skilled artisan.[2] (See, e.g., Defs.' FOF at FF149.) Defendants' anticipation case turns

[2] This Court has serious doubts that the Federal Circuit would agree that it is consistent with the existing law of anticipation to transform the disclosure of a piece of prior art based on what would have "stood out" to the skilled artisan. This sounds like the kind of concept more appropriate to an obviousness inquiry: it might be obvious to the skilled artisan that a numerical range may be reduced to a particular set of points within that range.

entirely on this proposition, and they have shown no legal support for it.

Defendants appear to use the Federal Circuit's phrase "at once envisage" to justify their transmutation of the prior art disclosure. Defendants try to justify their transformation of the EE range into seven specific options by characterizing it as within the process of the skilled artisan's envisaging. This Court need not reach the difficult question of how much transformation of the prior art disclosure should be accepted in the envisaging process because it is very clear that the limited class identified by Defendants – i.e., with EE dosages evenly divisible by 5 – is not expressly described in the '006 patent. Defendants have failed to demonstrate that the '006 patent expressly spells out a definite and limited class of contraceptive regimens. This alone prevents Defendants' anticipation argument from succeeding.

Defendants note that the Federal Circuit has distinguished the disclosure of a genus from a list of species. This is true and interesting, but the distinction does not add useful insight into the matter presently at issue – the EE dosage range in the '006 patent is a genus, not a list. Thus, on this subject, the Federal Circuit has stated:

> For the purposes of whether they are anticipatory, lists and genera are often treated differently under our case law. *Compare Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005) (rejecting "the notion that [a compound] cannot anticipate because it appears without special emphasis in a longer list") with *Atofina v. Great Lakes Chem. Corp.,* 441 F.3d 991, 999 (Fed. Cir. 2006) ("It is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus."). This distinction collapses when the class of compounds that falls within the genus is so limited that a person of ordinary skill in the art can at once envisage each member of this limited class. In that limited circumstance, a reference describing the genus anticipates every species within the genus. *See Perricone*, 432 F.3d at 1377. In this case, Gleave's arguments fail for two reasons. First, Wraight expressly lists every possible fifteen-base-long oligodeoxynucleotide sequence in IGFBP-2, and under our precedent, this list anticipates Gleave's claims. Second, even if we were to accept Gleave's invitation to treat Wraight as equivalent to the statement that

> one "could make antisense that targets IGFBP-2," which we decline to do, a person of ordinary skill in the art equipped with an IGFBP sequence is admittedly capable of envisioning how to make any antisense sequence.

In re Gleave, 560 F.3d 1331, 1337-1338 (Fed. Cir. 2009).

Gleave does not help Defendants. It states a rule (disclosure of a genus does not necessarily disclose every species within that genus), and an exception to that rule (for situations in which it is a limited genus of compounds). The rule certainly applies here; the question is whether the exception does. Read narrowly, this exception has no relevance to this case, since Defendants do not assert that the EE dosage range in the '006 patent is a genus of different compounds. Read more broadly, the exception would appear to apply to any genus with a limited number of members. If the exception is read in the broader sense, the EE dosage range in the '006 patent still does not fall within this exception, since a numerical range between two integers always contains within it an infinite set of rational numbers.[3]

Defendants do not point to any Federal Circuit case that states how to apply the genus/species anticipation rule in a case in which the genus is a numerical range containing an infinity of points, and the species is one point within that range. Defendants have shown no basis for this Court to conclude that the prior art genus expressly spells out a definite and limited class of contraceptive regimens. Defendants ask this Court to transform the range from a set with infinite members to one containing seven, based on the asserted selection preferences of a skilled artisan. Defendants show no foundation in Federal Circuit law for the Court to do so: Defendants have shown no controlling authority which establishes that such a transformation is

[3] "Algebra/Interval Notation" ("Between every two integers, there are an infinite number of fractional, or rational numbers"), wikibooks.org, http://en.wikibooks.org/wiki/Algebra/Interval_Notation (last visited Sept. 10, 2012).

permissible in conducting an anticipation analysis with a numerical range.

Defendants cite In re Petering, 301 F.2d 676, 681 (C.C.P.A. 1962), for the proposition "that it is not the mere number of compounds in this limited class which is significant here but, rather, the total circumstances involved. . ." It is worth noting that there is no Federal Circuit case ever which has cited Petering in support of a "total circumstances" inquiry in genus/species anticipation cases. Even if this Court were inclined to use Petering as the legal foundation for performing the Narrowing that Defendants seek, the Petering Court based its narrowing selection on the statements of preference in the prior art patent. Id. Defendants do not argue that the '006 patent contains statements of preference which select EE dosages evenly divisible by 5.[4] Defendants' "narrowing" effort has no precedent in Petering.

Moreover, as to Defendants' reliance on Petering, Plaintiffs aptly cite a decision that might be considered an "oldie but goodie:"

> We did not intend our *Petering* opinion or decision to become a precedent for the mechanistic dissection and recombination of the components of the specific illustrative compounds in every chemical reference containing them, to create hindsight anticipations with the guidance of an applicant's disclosures, on the theory that such reconstructed disclosures describe specific compounds within the meaning of section 102.

In re Ruschig, 343 F.2d 965, 974 (C.C.P.A. 1965). Defendants' approach to the '006 patent seems like just such dissection and recombination.

Defendants' "narrowing" approach looks very much like an attempt to rewrite the '006 patent to create a hindsight anticipation. Defendants argue: "Experts on both sides agree that,

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[4] Not to belabor this dead end but, as Plaintiffs point out, given the preference for a 35 µg EE dosage stated in the '006 patent, the OTCLO regimen does not fall within the group of preferred regimens. (Pls.' FOF ¶ 55.)

since the EE dosage moves in increments of 5 µg, there are only seven possible EE dosages within the range of 20-50 µg." (Defs.' FOF at FF 144.) As a matter of simple arithmetic, this statement is unfounded. Defendants cannot expect this Court to accept that, for example, an EE dose of 21 µg is impossible. Furthermore, the expert testimony cited by Defendants does not support this inference. Dr. Berga testified that "**if** we consider that there have to be 5 mcg increments," there would be seven possible dosages. (5/29/12 Tr. 105:23-24) (emphasis added). The cited testimony of Dr. Barnhart gives no explanation or justification for his selection of the seven dosages evenly divisible by 5, nor does he say that other doses are not possible. (5/30/12 Tr. 336:12-13.) Dr. Shulman testified that his selection of seven dosages relies on the assumption that estrogen dosage "moves in 5 mcg increments." (6/1/12 Tr. 579:11-13.) Not one of the cited experts testified that only seven dosages are possible within the EE range at issue.

Plaintiffs presented expert testimony which supported the proposition that the '006 patent discloses a very large number of potential contraceptive regimens – about 841 million.[5] (5/31/12 Tr. 506:25.) Defendants counter this only by proposing that they be allowed to limit the genus to species with characteristics which would stand out to the skilled artisan. As discussed, there is no support for the application of this "stand out" transformation of a genus in Federal Circuit law.

This Court concludes that Defendants' anticipation argument fails because it has not shown a basis in Federal Circuit law for the "narrowing" approach which changes a numerical range into seven discrete data points within that range. There is no legal basis for rewriting the

[5] Plaintiffs' calculation of 841 million regimens makes use of Defendants' reduction of the range of 20 to 50 µg to seven possible dosages.

prior art to create a hindsight anticipation. Defendants have failed to prove, by clear and convincing evidence, that claims 1 and 4 of the '815 patent are invalid as anticipated.

Furthermore, Plaintiffs contend, insightfully, that Defendants' narrow focus on the EE dosage alone – making the genus into one with only seven species – is supported neither by the language of the patent nor by the law of anticipation. As Plaintiffs suggest, under Federal Circuit law, the question is not whether the '006 patent describes a 25 µg EE dosage, but whether the '006 patent describes every element of the OTCLO regimen. It is by considering all the possible variables – not just estrogen dosage – that Plaintiffs find that the '006 patent contains 841 million possible regimens within its scope.

Moreover, consider the plain language of the specification in the '006 patent, which contains one of the statements of the 20 to 50 µg EE dosage range:

> According to the present invention, reliable contraception is achieved by administering for 21 successive days to a female a combination of an estrogen and a progestogen, for the first 5-8 days in a contraceptively effective daily dosage a progestogen equivalent in effect to about 0.065-0.75 mg of norethindrone in combination an estrogen equivalent in effect to about 0.02-0.05 mg of ethinyl estradiol; followed by the administration for 7-11 days, of a daily dosage of a progestogen equivalent in effect to about 0.25-1.0 mg of a norethindrone together with an estrogen equivalent in effect to about 0.02-0.50 mg of ethinyl estradiol; and followed by the administration for 3-7 days of a daily dosage of a progestogen equivalent in effect to about 0.35-2.0 mg of norethindrone in combination an estrogen equivalent in effect to about 0.02-0.05 mg of ethinyl estradiol, provided that the dosage of estrogen is kept constant in each phase during the 21-day cycle. The actual weight amount of the dosage at each dosage level will depend upon the estrogenic and progestogenic activity, respectively, of the components selected for the dosage units.
>
> The total number of days during which the progestogen and estrogen combinations are administered daily is 21. These are followed by 6-8 days which are free of hormone administration to approximate the natural 28-day menstrual cycle of the female. Day one of the cycle is defined as the first day of menstruation and the days are numbered sequentially thereafter until menstruation

> occurs again. The cycle usually lasts 28 days but it may be slightly longer or shorter. In actual practice a placebo or any other hormone-free agent such as, for example, iron supplements, may be administered during this period. Thus, in a preferred regimen, phase one would commence sometime between day 4 and day 6 of the menstrual cycle and last 5-8 days but preferably 7 days, phase two would last 7-11 days, preferably 7 days, while phase three would last 3 to 7 days, preferably 7 days.

'006 patent col.1 l.65-col.2 l.34. This language is not consistent with using only one variable to define the potential regimens. As Plaintiffs observe, Defendants have plucked one variable that defines the regimen (EE dosage) out of text which states a host of other variables.[6] The plain language of the specification supports Plaintiffs' position that Defendants' isolation of the one particular variable they are interested in, the EE range, is improper, since these paragraphs describe a much larger genus of regimens, defined by six major variables.

Defendants have failed to prove, by clear and convincing evidence, that claims 1 and 4 of the '815 patent are invalid as anticipated. Having found that Defendants' anticipation argument has failed, this Court need not reach the counterargument from Plaintiffs that the '006 patent states a preference for a 35 μg EE dosage, so that the OTCLO regimen is not a species within the genus of preferred regimens. The Federal Circuit cases on ranges with preferences and anticipation of a species by a genus do not appear to offer any clear rule on what to do when, as here, the species at issue is within the genus but not within the genus constrained by preferences.

B. Patent invalidity: obviousness

Defendants contend that claims 1 and 4 are obvious in view of the '006 patent. There is

[6] Plaintiffs point out that this specification section includes: "six major components comprising a particular triphasic oral contraceptive regimen: (1) phasing schedule, i.e., how many days for each phase; (2) steroid-free interval, i.e., the number of days that steroids are not administered; (3) estrogen type; (4) estrogen dosage; (5) progestogen type; and (6) progestogen dosage." (Pls.' FOF ¶ 50.) Estrogen dosage is thus only one variable out of six.

no dispute that the only difference between the patented method disclosed in claims 1 and 4 and the method disclosed in the '006 patent is that the patented method uses an EE dose of 25 µg, whereas the '006 patent teaches the use of an EE dose of 35 µg.

The first issue is the applicable law, which has recently changed. Defendants cite Iron Grip Barbell Co. v. USA Sports, Inc., 392 F.3d 1317, 1322 (Fed. Cir. 2004) (citations omitted):

> [W]here there is a range disclosed in the prior art, and the claimed invention falls within that range, there is a presumption of obviousness. But the presumption will be rebutted if it can be shown: (1) That the prior art taught away from the claimed invention; or (2) that there are new and unexpected results relative to the prior art . . .

Defendants acknowledge that this is no longer good law. It is clear that this principle was rejected to some extent[7] by the Federal Circuit in Eurand, Inc. v. Mylan Pharms., Inc. (In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.), 676 F.3d 1063, 1076 (Fed. Cir. 2012), in which the Court expressly cited Iron Grip as one of the cases which had used a *prima facie* obviousness principle. Pointing to this group of cases, the Federal Circuit stated: "those cases should not be interpreted as establishing a formal burden-shifting framework." Id. at 1077. Rather, the Federal Circuit reaffirmed that the guiding principle, established in Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530 (Fed. Cir. 1983), is that "courts [must] consider all objective evidence before reaching an obviousness conclusion." Cyclobenzaprine, 676 F.3d at 1076.

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[7] The extent to which it was rejected is a subject which can be, and surely will be, debated. The principle of a *prima facie* case of invalidity due to obviousness in litigation has been clearly rejected. It is not at all clear, however, what courts should now do with the fact that a claimed invention falls within a range disclosed in the prior art. It seems quite possible that the instant case will be appealed and will offer the Federal Circuit the opportunity to give further guidance on this question.

In light of Cyclobenzaprine, then, the fact that the claimed invention falls within a range disclosed in the prior art has no special significance to the obviousness inquiry. It is but one fact to be weighed with the other evidence in performing the inquiry under 35 U.S.C. § 103(a), which requires that the Court determine "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." The patent is presumed valid, and the burden remains on Defendants to prove the invalidity of the patent by clear and convincing evidence.

There is no dispute that the prior art references at issue were before the examiner during prosecution. The Federal Circuit has recently clearly stated that this fact does not alter the burden of proof of invalidity:

> Whether a reference was previously considered by the PTO, the burden of proof is the same: clear and convincing evidence of invalidity. . . The burden does not suddenly change to something higher—"extremely clear and convincing evidence" or "crystal clear and convincing evidence"—simply because the prior art references were considered by the PTO. In short, there is no heightened or added burden that applies to invalidity defenses that are based upon references that were before the Patent Office. The burden is always the same, clear and convincing evidence.

Sciele Pharma, Inc. v. Lupin Ltd., 684 F.3d 1253, 1260 (Fed. Cir. 2012).

> The foundation of the law of obviousness is the statute, § 103:
>
> A patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

35 U.S.C. § 103(a). "It is well-settled that obviousness is a legal question based on underlying

factual determinations." Iron Grip, 392 F.3d at 1323.

> [F]actual determinations relevant to the obviousness inquiry include: (1) the scope and content of the prior art; (2) the differences between the claimed invention and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations, if any, such as commercial success, unexpected results, copying, long-felt but unresolved need, and the failure of others to develop the invention.

Syntex (U.S.A.) LLC v. Apotex, Inc., 407 F.3d 1371, 1378 (Fed. Cir. 2005).

Defendants offer three basic arguments to prove the invalidity of the patent: 1) the patentee did not provide any scientifically valid evidence that OTCLO exhibits unexpected results; 2) it would have been obvious to the skilled artisan to take the regimen in the '006 patent and reduce the EE dosage by 10 µg; and 3) Plaintiffs' other asserted secondary considerations are unsupported.

These arguments turn on a number of factual disputes. The parties do not dispute the level of ordinary skill in the art, nor that the sole difference between the claimed regimen and that of the prior art, specifically the OTC regimen disclosed in the '006 patent, is a 10 µg decrease of EE dosage to 25 µg.

1. The scope and content of the prior art

The parties do not dispute that, in 1998, the skilled artisan in the field of oral contraceptives was faced with the problem of estrogen side effects, which were known to decrease as estrogen dosage decreased. As a corollary, then, it is undisputed that skilled artisans wanted to create OC regimens with lower estrogen dosages, and that the form of estrogen that was generally used was EE. At the time, many OC regimens had dosages of 30 µg EE or greater, but a few, known as "ultra low dose of estrogen" regimens, used EE dosages as low as 20 µg. In 1998, there were four such regimens available in the United States: Loestrin 1/20, Alesse,

Estrostep and Mircette. These facts are undisputed.

At issue is what was known in 1998 about the effect on cycle control of lowering the EE dosage below 30 µg. Significantly, Defendants concede that the skilled artisan, as of December 1998, would have viewed a 20 µg EE dosage as unacceptably raising the risk of poor cycle control: "the accepted view as of 1998 [was] . . . that 20 µg EE presented the problem of possibly increased breakthrough bleeding . . ." (Defs.' Br. 82.) Moreover, Defendants concede that the skilled artisan would have believed that "20 µg was too low of a dose." (Id.) At issue, then, is what the skilled artisan would have thought about a 25 µg dosage. Defendants contend that a 25 µg EE dosage was an obvious choice. The evidence does not support this.

There appeared to be a consensus among the experts that the skilled artisan, in 1998, would have known about the results of three principal research studies on cycle control characteristics of ultra low dose of estrogen regimens: Endrikat, Akerlund, and Tuimala. Each of these studies compared two OC regimens that were identical except for the EE dosage, and all three studies compared a regimen with a 30 µg EE dosage to a regimen with a 20 µg EE dosage.

The 1997 study by Endrikat and colleagues, published in the journal, "Contraception," compared two regimens containing the progestin gestodene, and either 30 µg or 20µg EE. (Ex. JTX 17.) The 20 µg regimen produced cycle control inferior to the 30 µg regimen at a statistically significant level. (Id. at 133.) The article states that these results confirm findings in two other similar studies. (Id. at 136.) The study concludes that, for women with a history of cycle control problems, the 30 µg regimen was preferred over the 20. (Id. at 137.) The Endrikat study supports Plaintiffs' position that the skilled artisan would have expected a reduction in EE dosage to be associated with inferior cycle control.

The 1997 Akerlund study reported similar results, using regimens with a different progestin, desogestrel, with 30 µg and 20 µg of EE: it found "less effective cycle control" for the 20 µg regimen. (Ex. DTX 300 at 65.)

An earlier study, the 1987 Tuimala study, also used regimens with desogestrel, with 30 µg or 20 µg of EE, but found no differences in cycle control. (Ex. JTX 028.) Unlike the Akerlund and Endrikat studies, which were "head-to-head" studies in which the experimental method was constant across the two regimen groups, the Tuimala study compared two separate studies. (Id.) It was the consensus of the experts at trial that, other things being equal, "head-to-head" studies provided more reliable information than comparative studies did.[8] Thus, the two relevant head-to-head studies in 1997 showed that 20 µg regimens produced cycle control inferior to 30 µg regimens.

More importantly, the Akerlund and Endrikat studies support Plaintiffs' contention that these studies taught away from the strategy that Defendants say would have been obvious (to select the OTC regimen and reduce the EE dosage by 10 µg.) The Akerlund and Endrikat studies appear to suggest that doing so will result in inferior cycle control – thus discouraging the skilled artisan from simply reducing a known regimen's EE by 10 µg. This is modest but substantial evidence of teaching away.

The record includes a number of review articles and guides to oral contraceptives for the prescribing physician which generally support the proposition that the skilled artisan would have expected a decrease in estrogen dosage to lead to a decrease in cycle control. Both sides

[8] Notably, Defendants' expert Dr. Berga agreed that the skilled artisan would have viewed Akerlund as a more reliable study than Tuimala. (5/30/2012 Tr. 216:2-5.)

presented evidence from experts in contraception on the question of whether the skilled artisan, as of the critical date, would have expected a deterioration in cycle control when lowering the EE dose from 35 µg to 25 µg. Defendants point out that low-estrogen regimens were known in the art well before 1998, and cite to the testimony by Dr. Darney in which he admits that, in approximately 1993, he had written a book chapter which stated:

> Although the list of oral contraceptives is long, low-dose pills with 20 to 35 mcgs of ethinyl estradiol combined with .15 to one mg of a progestogen are appropriate for the majority of prescribing situations.
> . . .
> Only under unusual circumstances is the dose greater than 35 mcgs of ethinyl estradiol, and for some women it is as low as 20 mcgs.

(6/4/12 Tr. 792:18-21, 793:13-15.) This does not appear to help Defendants much. While Dr. Darney recognized in 1993 that there are OCs available with an estrogen dosage as low as 20 µgs, this dose at the low end is recommended only for "some women." Dr. Darney does not define the size of this subgroup, but, from the context, the suggestion seems to be that this is not typical. The 1993 Darney reference does not suggest that an EE dosage at the low end of the range is appropriate for most women. Furthermore, reading just a bit farther in the reference, it is clear that Darney has qualified these statements so as to make them consistent with his later statements:

> Breakthrough bleeding commonly occurs during the first 2 or 3 months of oral contraceptive use. Its incidence depends on the dose of synthetic estrogen (increased with preparations containing <30 µg) and type of progestogen (decreased with the newer progestogens, even with estrogen doses <30 µg.)

(Ex. DTX 282 at 479.) This reference is, however, somewhat helpful to Defendants: it suggests an interaction between choice of progestogen and reduction of the estrogen dosage that can mitigate the impact of reduced estrogen dosage on cycle control. It does not, however, show that

it was known in the art in 1998 that the use of norgestimate would allow a 10 µg reduction in EE dosage without a deleterious impact on cycle control.

Aside from this 1993 article by Dr. Darney, the medical literature of record consistently reflected a straightforward belief that decreases in EE dosage produced decreases in cycle control. Moreover, Defendants' expert Dr. Barnhart testified that, as a general concept, the art believed that reducing estrogen dosage is associated with increased bleeding problems. (5/30/12 Tr. 370:15-20.) That alone is sufficient evidence, but there are numerous pieces of evidence supporting this view in the record, and they will be briefly enumerated here.

To start, Dr. Darney testified that he wrote an article giving oral contraceptive practice guidelines, published in 1987, which stated: "The frequency of breakthrough bleeding and spotting has been shown to increase as the estrogen dose decreases." (6/1/12 Tr. 629:18-630:15.) Dr. Darney described this statement as "a ubiquitous observation." (Id. at 630:18.)

Plaintiffs also cite a 1998 article in the journal, "Contraception," titled, "Oral Contraceptive Estrogen Dose Considerations," which states:

> By providing endometrial support, the estrogen component of OCs prevents breakthrough bleeding. As OC estrogen doses decline, therefore, cycle control also declines. Accordingly, 20-µg EE OCs have been found to have higher rates of breakthrough bleeding and spotting than 30- and 35-µg formulations . . .

(Ex. PTX 163 at 16S.) Plaintiffs also cite another 1998 article, by Darney and Klaisle, in the journal, "Dialogues in Contraception," titled, "Contraception-Associated Menstrual Problems: Etiology and Management," which states:

> By providing endometrial support, the estrogen component of OCs prevents breakthrough bleeding. As OC estrogen doses decline, cycle control decreases. OCs containing 20 mcg estrogen have been found to have higher rates of breakthrough bleeding and spotting than formulations containing 30 or 35 mcg of

estrogen.

(Ex. JTX 16 at 2.)

Dr. Berga offered a selective and misleading quote from a 1997 survey article[9] on oral contraceptives which stated, "The bottom line is that you can lower the estrogen dose quite far and keep cycle control." (5/28/12 Tr. 105:1-3.) The problem is that Dr. Berga failed to give the entire sentence, which, in its entirety, is as follows: "The bottom line is that you can lower the estrogen dose quite far and keep cycle control when the progestational agent is providing an additional endometrial support function." (Ex. DTX 270 at 9.) Moreover, the sentence which follows this one states: "One area where lower-dose preparations are not as effective as 50 mcg preparations is early cycle control." (Id.) The article then describes one study that found decreased cycle control associated with decreased dosages of estrogen and progestin. (Id.)

Dr. Berga's selective quoting from the 1997 survey article is misleading. The fairest reading of the "Trends" article is that it shows uncertainty about whether cycle control for 20 mcg regimens is as good as cycle control for regimens with higher EE dosages. The article quotes from one physician who said that some clinicians shied away from prescribing 20 mcg estrogen formulations because of concerns over breakthrough bleeding, but that no head-to-head comparison of 20 mcg formulations with 30 mcg or 35 mcg formulations had been done. (Ex. DTX 270 at 8.) The article cites a study of one particular regimen which used a 20 mcg EE dose which reported good cycle control. (Id. at 9.) All in all, the article teaches that cycle control is a function of the dosage of both the estrogen and progestin components. It would not be a fair

[9] The article, exhibit DTX 270, is in the January 1997 issue of "The Contraception Report." The article is titled: "Trends in Oral Contraceptive Utilization and Performance: Looking to the Future." No author is named. At trial, this was referred to as the "Trends" article.

reading of this article to say that it provides support for the proposition that, in January of 1997, the art believed that one could make a single change to a regimen, lowering the regimen's EE dosage to 20 mcg, and maintain the same level of cycle control.

In 1997, the International Journal of Fertility published an article by Dr. Darney. (Ex. PTX 117.) Discussing breakthrough bleeding ("BTB"), Dr. Darney wrote:

> BTB is related to the dose, potency, and ratio of the estrogen and progestin in the OC formulation, as well as to individual physiologic response. However, information about different OC preparations and how they affect menstrual problems has been confusing. . .
>
> The frequency of BTB and spotting has been shown to increase as the estrogen dose decreases. . . . There is evidence that the difference between 30 µg EE and 20 µg EE is meaningful in terms of BTB.

(Id. at 162-163.) The article then discusses the Akerlund study as the evidence referred to. (Id. at 163.)

The parties offered other articles, textbooks, and the like: 1) the article by Burkman and Shulman, published in 1998 in "Contraception," titled "Oral Contraceptive Practice Guidelines" (estrogen "maintains the endometrium and prevents breakthrough bleeding;" "[v]ariations in estrogen dose among formulations containing <50 µg EE may also affect cycle control") (Ex. PTX 102 at 35S); and 2) the article by Kaunitz, published in 1998 in "Contraception," titled "Oral Contraceptive Estrogen Dose Considerations" (Ex. PTX 163.) Kaunitz reviewed a number of research studies and concluded that "20 µg EE OCs have been found to have higher rates of breakthrough bleeding and spotting than 30- to 35-µg EE formulations." (Id. at 16S.)

Lastly, in an editorial published in 2001, Dr. Ian Thorneycroft wrote:

> Data comparing cycle control in women taking 20- and 35-mcg EE preparations are limited and inconsistent. The variation is due to the lack of true head-to-head

> comparisons of factors affecting tolerability and continuation rates in addition to the disparate definitions of abnormal bleeding. Products compared in some studies differ with regard to both estrogen dose and progestin component and phasing. However, when OC formulations with the same progestin component are compared, the lower the dose of estrogen, the more diminished is the cycle control.

(Ex. PTX 228 at 3.) Although this paragraph was published in 2001, the studies which it cites were all in the prior art as of the critical date, and, based on the evidence of record before this Court, it appears to be a fair assessment of the state of the art as of the critical date. As of the critical date, the skilled artisan believed that, generally, decreasing estrogen dosage results in decreased cycle control.

2. The factual foundation for unexpected results

The other major factual issue in this case is the question of whether the OTCLO regimen produced cycle control equal to that produced by the OTC regimen. At trial, Defendants made elaborate efforts to raise doubt about Table 5 in the patent, and to raise doubt about any research evidence suggesting that OTC and OTCLO produced equivalent cycle control. Nonetheless, Defendants' expert Dr. Berga admitted that "there is no clinically meaningful difference in cycle control between Ortho Tri-Cyclen and Ortho Tri-Cyclen Lo." (5/30/12 Tr. 223:14-20.) Dr. Berga also testified that the reduction of EE dosage from the 35 µg to 25 µg "did not result in a substantial loss of cycle control." (5/30/12 Tr. 224:1-5.) She admitted as well that the physiological effect of the two estrogen dosages on a woman's reproductive system is "the same." (Id. at 90:9-20.) In the face of Dr. Berga's admission on the stand that, in reality, there is no clinically meaningful difference in cycle control between OTC and OTCLO, and that the physiological effects of the two EE dosages are the same, all of Defendants' efforts to cast doubt

on the validity of Table 5 are immaterial. Indeed, the Court views these admissions as conclusive evidence that, for the purpose of resolving the instant disputes, OTC and OTCLO produce equivalent cycle control. The Court will now discuss other evidence and arguments pertaining to this issue, but no further evidence is needed to resolve this factual dispute.

The inference that OTC and OTCLO produced equivalent cycle control is supported by other evidence, most notably the K90 study, some later publications, and evidence comparing the commercial success of the two regimens.

Defendants put much effort into attacking evidence which compares the cycle control of OTCLO to OTC which is not based on a "head-to-head" study – a study in which cycle control data on two or more contraceptive regimens is obtained through one standard methodology. Defendants have persuaded this Court that, other things being equal, the results of a head-to-head study deserve more weight than the results of a study in which experimental groups did not share a common research method. There is no dispute that the study known as "the K90 study" was such a head-to-head study. There is also no dispute that the study found no statistically significant differences on cycle control measures between the OTC and OTCLO regimens.

Defendants deny, however, that the K90 study actually shows what it appears to show: there is no significant difference in cycle control between OTCLO and OTC. Defendants protest that the K90 study did not have large enough sample sizes to demonstrate statistically significant differences. Again, this criticism might have some legal significance if Plaintiffs bore the burden of proof, but they do not. Defendants' position, in short, is that the K90 study still isn't good enough to prove the unexpected results. Again, Plaintiffs do not bear any burden of proof of validity. Defendants' complaint, that the K90 study did not have large enough sample sizes to

reveal the allegedly true differences in cycle control between the regimens, even if credited, does not help them carry their burden of proving invalidity by clear and convincing evidence. Defendants' criticism of the K90 study, if credited, does no more than suggest that the K90 study is not the optimal study and that, were it to be weighed against a hypothetical perfect study which is not in the record presently before this Court, it would deserve less weight. This does not help Defendants carry their burden of proof of invalidity.

The inference that OTC and OTCLO have comparable cycle control is supported by the evidence that later artisans believed this to be true. An article by David and colleagues, published in 2006 in "Mayo Clinic Proceedings," titled "Hormonal Contraception Update," states that the OTCLO regimen provides "both the reduced estrogenic effects of the 20-µg EE formulations and the better bleeding profiles of the 30- to 35-µg EE formulations." (Ex. PTX 118 at 949.) The article observed that the OTCLO formulation allowed a reduction in estrogen "without sacrificing cycle control." (Id.) Mishell and Sulak wrote an article arriving at the same conclusions, published in 2002 in "Dialogues in Contraception," titled, "Bleeding Patterns with Hormonal Contraceptives and IUDs." (Ex. PTX 183.) These authors stated: "There are some exceptions to the general relationship between EE dose and cycle control, because the type of progestin and the estrogen-progestin ratio in an OC formulation also may have effects on cycle control." (Id. at 2.) They identified OTCLO as one such exception, and stated that it showed an "excellent cycle-control profile." (Id.) This evidence supports the inference that cycle control is comparable.

Lastly, the evidence regarding the commercial success of OTCLO is not consistent with the view that OTCLO was not at least comparable to OTC. The historical data showing total

prescriptions by year shows that, starting in 2002, OTCLO prescriptions rose in a steady and fairly linear fashion until 2006, reaching a high of about 300 million prescriptions annually. (Ex. DTX 433.) Annual totals then declined to about 200 million in 2008, dropping somewhat more sharply in 2009. (Id.) During this time, annual prescriptions for OTC continually dropped – and did so precipitously between 2003 and 2004. (Id.) If, in fact, OTCLO produced inferior results, one would not expect the annual total number of prescriptions to grow every year for four years. Also, it would be difficult to square the fact that over 100 million prescriptions for OTCLO were written each year for seven years running with the idea that OTCLO actually produced inferior cycle control, as the skilled artisan would have expected in 1998. If OTCLO actually resulted in a loss of cycle control, relative to OTC, one might expect to have seen perhaps an initial burst in prescriptions for OTCLO, and a dip in prescriptions for OTC, followed by a decrease to zero in prescriptions for OTCLO, and an associated rebound for OTC. This is not what the data shows.

Defendants have unsuccessfully attempted to raise doubt that OTC and OTCLO have comparable cycle control. Ultimately, this Court need not sift through the details of Defendants' attacks on Plaintiffs' evidence about the cycle control properties of OTCLO. Even if every criticism made by Defendants is credited, these criticisms carry little weight in view of the facts that the head-to-head K90 study showed no significant difference in cycle control between OTCLO and OTC and, most significantly, that Defendants' expert testified that there was no clinically meaningful difference in cycle control between the regimens. Defendants have not succeeded in persuading this Court that Plaintiffs have no support for their claim of unexpected results. Having considered all the evidence at trial, this Court finds that there is no clinically meaningful difference in cycle control between OTC and OTCLO.

3. Defendants' legal arguments regarding obviousness

Having made the necessary underlying factual determinations, this Court now considers Defendants' legal arguments that the '815 is invalid as obvious. Defendants first argue that the patentee did not provide any scientifically valid evidence that OTCLO exhibits unexpected results. This argument suffers from major defects. In considering it, the first question is the legal foundation for this challenge. Defendants do not lay an adequate legal foundation for the proposition that the failure to provide scientifically valid evidence that OTCLO exhibits unexpected results should lead this Court to find the patent invalid as obvious.

Defendants do attempt to lay a legal foundation for this argument, trying to insert a scientific validity requirement into Federal Circuit law, but it is unpersuasive, for several reasons. One problem for Defendants is their failure to distinguish the legal framework of prosecution from that of litigation. Defendants only cite four cases in support of their position, and, for two of those four, Defendants fail to recognize that they are patent prosecution cases which do not use the legal standard applicable to district court litigation. Defendants begin their discussion of the law by citing In re Geisler, 116 F.3d 1465, 1469 (Fed. Cir. 1997). At the outset, this is problematic. Geisler is an appeal of a decision of the Board of Patent Appeals and Interferences, which had ruled on an appeal of an examiner's obviousness rejection during prosecution. Id. at 1468. One of the main points made by the Federal Circuit in Cyclobenzaprine is that the obviousness inquiry used by the Board of Patent Appeals and Interferences in considering a decision made during prosecution differs, for good reason, from that used in litigation which originates in the federal courts. 676 F.3d at 1080 n.7. The Federal Circuit's discussion in footnote 7 of the differences in legal framework makes quite clear that they are substantial.

Geisler is not irrelevant to the instant case, but its principles must be considered in terms of the context of prosecution. To apply Geisler to litigation without considering the difference in context is an error.

This distinction is not merely academic. As explained in Cyclobenzaprine:

> Unlike in district court litigation, a burden-shifting framework makes sense in the prosecution context. . . . Courts should not apply the burden-shifting framework for patentability appeals to invalidity determinations appealed from a district court, however, because the prosecution and litigation contexts are distinct.

Id. at 1080 n.7. If this Court applied Geisler in the instant case, it would thus be reversible error. Furthermore, Cyclobenzaprine explains that, while the question during prosecution is patentability, shown by the applicant by a preponderance of the evidence, the question in litigation is validity, shown by the challenger by clear and convincing evidence. Id.

Similarly, Defendants cite In re Inland Steel Co., 265 F.3d 1354, 1366 (Fed. Cir. 2001), another appeal in the prosecution context from a decision of the Board of Patent Appeals and Interferences.

Defendants also cite McNeil-PPC, Inc. v. L. Perrigo Co., 337 F.3d 1362, 1370 (Fed. Cir. 2003). McNeil is a Hatch-Waxman case involving an challenge to a patent based on, *inter alia*, invalidity due to obviousness. Id. In McNeil, the Federal Circuit held that the district court had properly discounted the evidence of unexpected results, stating: "Finally, the court found that the results of clinical studies adduced by McNeil were inconsistent, not shown to be reproducible, and did not include comparative data vis-a-vis placebos or other antidiarrheal/antiflatulent combinations necessary to demonstrate unexpected or synergistic effects." Id. This single sentence is all that the Federal Circuit stated on this subject in McNeil. Based on this and other

evidence, the Federal Circuit concluded that the district court correctly found the claims at issue invalid as obvious. Id. at 1371. The discounted evidence of unexpected results was one element among others which supported the conclusion of obviousness. McNeil thus stands for the proposition that a district court may, where appropriate, discount clinical studies offered as evidence of unexpected results if they are inconsistent, not reproducible, or lack comparative data "necessary to demonstrate unexpected or synergistic effects." Id. McNeil does not, however, establish that any of these characteristics are required to demonstrate unexpected results. The fact that a district court may discount evidence of unexpected results, where appropriate, when weighing the evidence of obviousness, does not imply any legal requirements as to how unexpected results must be demonstrated.

Lastly, Defendants cite Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1371 (Fed. Cir. 2007) for the unremarkable proposition that "in order to properly evaluate whether a superior property was unexpected, the court should have considered what properties were expected."

In sum, Defendants have not persuaded this Court that a patentee faced with a validity challenge must provide evidence of unexpected results that passes muster under undefined high standards of scientific validity.

Of great concern to this Court is an implicit shifting of the burden of proof that lurks in Defendants' position. Defendants appear to argue that, faced with a validity challenge, the patentee bears a burden of proof in regard to unexpected results, as if the patentee must prove something to show the patent valid. If that is Defendants' argument, it is dead wrong: Defendants bear the burden of proof of invalidity by clear and convincing evidence. The patentee has no obligation to prove anything in regard to validity at this juncture. The patent is

presumed valid. 35 U.S.C. § 282.

For example, consider Defendants' argument that Plaintiffs failed to offer evidence of what cycle control result the skilled artisan would have expected from OTCLO. Even if true, to repeat, at this juncture, Plaintiffs have no obligation to prove what the skilled artisan would have expected from OTCLO. Rather, again, Defendants bear the burden of proof of invalidity. Defendants' suggestion that Plaintiffs are vulnerable because they have failed to show what a skilled artisan would have expected is simply misdirection – an attempt to distract attention from their own obligation to prove invalidity.

Defendants proceed with their unexpected results argument by offering the contention that the applicant "obtained allowance of the '815 patent solely on assertions of unexpected results." (Defs.' FOF at 14.) Defendants' argument contains the following propositions: 1) the applicant "obtained allowance of the '815 patent solely on assertions of unexpected results" (Defs.' FOF at 14); 2) the applicant relied on Table 5 to persuade the examiner of the unexpected results; and 3) Table 5 does not constitute scientifically valid proof of unexpected results.

This Court queries: for purposes of discussion only, even if Defendants persuaded this Court that all three propositions are true, where is this going? Absent an inequitable conduct argument – which Defendants do not make –, what is the legal significance of a finding that Table 5 does not constitute scientifically valid proof of unexpected results? Given that Dr. Berga admitted that there is no clinically meaningful difference in cycle control between the OTC and OTCLO regimens, the scientific validity of Table 5 would appear to be irrelevant. Moreover, as noted above, there appears to be hidden in this argument an attempt to shift the burden of proof at this juncture onto Plaintiffs.

In short, for any number of reasons, Defendants' attack on the scientific validity of the evidence of unexpected results fails to show this Court any basis to find the '815 patent invalid as obvious.

Defendants next raise the argument that it would have been obvious to the skilled artisan to take the regimen in the '006 patent and reduce the EE dosage by 10 µg. They begin by quoting Dystar Textilfarben GmbH v. C.H. Patrick Co., 464 F.3d 1356, 1360 (Fed. Cir. 2006): "We thus consider whether a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and whether there would have been a reasonable expectation of success in doing so." Defendants contend that the skilled artisan would have had a reasonable expectation of success in developing a contraceptive by reducing the OTC regimen's EE dosage by 10 µg. Defendants first address the question of whether the skilled artisan would have believed that the OTCLO regimen would be effective as a contraceptive. Although there is some dispute about this issue,[10] this Court need not reach it, because deciding the cycle control issue alone is sufficient to determine the outcome of the inquiry into a reasonable expectation of success.

The question of whether the skilled artisan would have had a reasonable expectation of

[10] This dispute centers on the question of what dosage of norgestimate the skilled artisan would have believed to be the minimum inhibitory dosage – the minimum level for contraceptive efficacy. This dispute turns on factual questions involving the content of the prior art, particularly the Eyong study, and what the skilled artisan would have understood about minimum inhibitory dosage, and therefore whether there would have been a reasonable expectation of contraceptive efficacy with the OTCLO rgimen. The Court need not decide this factual dispute because Defendants have failed to prove that the skilled artisan would have had a reasonable expectation that the OTCLO regimen would have comparable cycle control to the OTC regimen. There is thus no need to reach the question of whether the skilled artisan would have had a reasonable expectation of contraceptive efficacy with the OTCLO regimen.

success with the OTCLO regimen may be decided from the inquiry into whether the skilled artisan would have believed that changing the OTC regimen by reducing the EE dosage from 35 µg to 25 µg would have resulted in a deterioration in cycle control. Defendants contend that framing the question in this way, as Plaintiffs have, is "improper." (Defs.' Br. 75.) Defendants argue that cycle control is not a claim limitation, and that the reasonable expectation of success must be with regard to achieving the claimed invention. Thus, Defendants argue, all that is required to show obviousness is a reasonable expectation of success in combining the prior art to create a contraceptive regimen.

The problem for Defendants is that they do not provide persuade that cycle control should be disregarded in this obviousness inquiry. The cases they cite do not support the proposition that the inquiry into teaching away and unexpected results is limited to the subject matter of the claims alone. Defendants seek to support their legal position first by pointing to the use of the phrase "the claimed invention" in In re Kubin, 561 F.3d 1351, 1360 (Fed. Cir. 2009), but Defendants do not argue that Kubin actually holds that the inquiry into teaching away and unexpected results is limited to the subject matter of the claims alone – and, in any case, Kubin does not hold that. Defendants next cite Aventis Pharma S.A. v. Hospira, Inc., 675 F.3d 1324, 1330 (Fed. Cir. 2012), but that case stands for the proposition that, in the context of claim construction, courts should hesitate to read limitations into claims when not required by the language of the claims or the specification. There is no claim construction dispute presently before this Court, and Aventis is inapposite. Lastly, Defendants cite Tyco Healthcare Group LP v. Mut. Pharm. Co., 642 F.3d 1370, 1374 (Fed. Cir. 2011), but the aspect of the decision Defendants quote does not stand for any proposition useful to their argument here. The cases

cited by Defendants do not provide an adequate legal foundation for their contention that "a reasonable expectation of acceptable cycle control is irrelevant to the determination of whether a reasonable expectation of success existed with respect to claims 1 and 4 of the '815 patent . . ." (Defs.' Br. 76-77.)

On this subject, this Court observes that the plain language of the '815 patent does not support Defendants' assertion that cycle control is irrelevant. First, the specification of the '815 patent makes very clear that the inventor believed that what was invented was an oral contraceptive regimen with unexpectedly good cycle control. In the "Background of the Invention" section, the specification has an extensive discussion of the issue of cycle control and estrogen dosage. '815 patent col.1 l.12-col.3 l.13. Next, in the "Summary of the Invention" section, the specification states: "Applicants have surprisingly discovered for this triphasic regimen and as demonstrated below, that the reduced level of estrogen administration does not result in a commensurate reduction in cycle control." '815 patent col.3 ll.41-44. In the "Detailed Description of the Invention" section, the specification describes in extensive detail the cycle control results from five comparative research studies. '815 patent col.6 l.10-col.13 l.53. In short, from the specification's description of these five studies, it is unmistakable that the patentee understood the invention to be a contraceptive regimen that provided equivalent cycle control to prior art regimens.

The point here is that Defendants' position is predicated on the proposition that good cycle control is not part of the invention. This proposition is inconsistent with the plain language of the specification.

The Federal Circuit has made clear that it is not the claims alone that describe the subject

matter of the invention:

> The claims, of course, do not stand alone. Rather, they are part of "a fully integrated written instrument," *Markman*, 52 F.3d at 978, consisting principally of a specification that concludes with the claims. For that reason, claims "must be read in view of the specification, **of which they are a part.**" *Id.* at 979.

Phillips v. AWH Corp., 415 F.3d 1303, 1315 (Fed. Cir. 2005) (emphasis added). Reading the '815 patent as a fully integrated written instrument, the patentee has clearly and unmistakably expressed the understanding that what was invented was an oral contraceptive method that produced cycle control equal to that in the prior art. Having examined both the law and the language of the '815 patent, this Court finds that Plaintiffs have failed to point to support for their contention that cycle control is irrelevant to a reasonable expectation of success in practicing the invention.

Defendants next argue that the skilled artisan would have been motivated to combine the prior art teachings so as to change the OTC regimen by reducing the EE dosage 10 µg. There is no dispute that, as Defendants contend, a skilled artisan in 1998 was interested in lowering estrogen dosages so as to reduce estrogenergic side effects, and that at least four regimens with 20 µg EE dosages had received FDA approval. Plaintiffs do not dispute that the skilled artisan would have been motivated to formulate an OC regimen with a lower EE dosage. Plaintiffs' case, however, is that the skilled artisan would have expected such a change to result in a clinically significant decrease in cycle control – a factual matter which this Court has decided in Plaintiffs' favor.

Defendants also contend that Plaintiffs have failed to point to references that taught away from the OTCLO regimen. The Federal Circuit applies the following principles to the inquiry

into teaching away:

> A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. A reference does not teach away, however, if it merely expresses a general preference for an alternative invention but does not criticize, discredit, or otherwise discourage investigation into the invention claimed.

Depuy Spine, Inc. v. Medtronic Sofamor Danek, Inc., 567 F.3d 1314, 1327 (Fed. Cir. 2009) (citations omitted). Plaintiffs contend that, as of the critical date, it was commonly believed that reducing EE dosage would lead to decreased cycle control, and that this would discourage the skilled artisan from further reducing the EE dosage of the OTC regimen. This Court has found that, as of the critical date, the direct connection between estrogen dosage and cycle control was generally accepted in the art. This would discourage a person of ordinary skill from following the path taken by the applicant – reducing the EE dosage of the OTC regimen. The evidence of record clearly supports finding that numerous prior art references taught away from the invention.

Furthermore, the evidence shows that it was accepted scientific knowledge in 1998 that reducing EE dosage was associated with decreased cycle control. The patentee worked in a direction that was contrary to that knowledge. "Proceeding contrary to the accepted scientific knowledge is strong evidence of nonobviousness." Santarus, Inc. v. Par Pharm., 2012 U.S. App. LEXIS 18592, *55 (Fed. Cir. Sept. 4, 2012) (citation omitted).

Defendants offer nothing persuasive to counter this demonstration of teaching away. Defendants do argue that the '006 patent does not teach away from a reduction in EE dosage, but this is of no significance. There is no legal requirement that every relevant piece of prior art teach away from an invention.

Lastly, Defendants contend that Plaintiffs have failed to demonstrate various secondary considerations. Among these, Defendants first target industry praise. As discussed *supra*, the later article by Mishell and Sulak praised OTCLO, stating it provided an "excellent cycle-control profile." (Ex. PTX 183 at 2.) This Court finds that the art has praised the OTCLO regimen.

The Mishell and Sulak article discusses the OTCLO regimen in a way particularly convincing of nonobviousness: "Similarly, [norgestimate] has greater progestational activity with less androgenic activity than NET and LNG. This attribute may contribute to the excellent cycle-control profile of [OTCLO]." (Id.) It is noteworthy that the authors offer a hypothesis (about the mechanism of action) to attempt to explain the cycle control profile of OTCLO. If this result was obvious in 1998, why were scientists in 2002 trying to explain why it happened?

Furthermore, Mishell and Sulak characterized OTCLO as an exception to the general rule about the effect of estrogen dosage on cycle control. Thus, the evidence of record shows that, before the invention of OTCLO, the art generally perceived a correlation between estrogen dosage and cycle control; after the invention, OTCLO was viewed as an exception to that rule. This supports the view that the cycle control characteristics of OTCLO were unexpected and that it would not have been obvious to the skilled artisan to follow the path of the inventor.

There is no dispute that OTCLO has been a commercially successful pharmaceutical product. Defendants contend that this factor deserves less weight as an objective indicator of nonobviousness because of the existence of blocking patents. Merck & Co. v. Teva Pharms. USA, Inc., 395 F.3d 1364, 1377 (Fed. Cir. 2005). Although the parties do not dispute that the Pasquale patents covered the OTCLO regimen, the parties dispute whether the rationale of Merck applies in this case. The Merck Court explained its discounting of commercial success as

follows: "Because market entry by others was precluded on those bases, the inference of non-obviousness of weekly-dosing, from evidence of commercial success, is weak." Id. In the instant case, there has been no demonstration that market entry by others was precluded. To the contrary, it appears undisputed that at least two low-estrogen regimens entered the market in 1998. As Plaintiffs observe, the active ingredients in the OTCLO regimen were not under patent protection in 1998. Because market entry by others was not precluded, the rationale of Merck is inapplicable here.

Furthermore, this Court finds unpersuasive Defendants' arguments that the commercial success is merely a product of the amount of money spent on promotion. In the OC field, promotional efforts are directed at learned intermediaries. These physicians would not have prescribed OTCLO had they not believed that the product was appropriate for their patients. This Court thus concludes that Plaintiffs have demonstrated that OTCLO has been commercially successful, and weighs this as supporting a finding of nonobviousness.

The evidence supporting the secondary consideration of unexpected results has already been considered: the evidence of record strongly supports the conclusion that the OTCLO regimen produced cycle control comparable to that produced by OTC, and that this result was unexpected. In this case, this Court finds the secondary considerations evidence to be highly relevant to the finding of nonobviousness. As the Federal Circuit has stated:

> The objective indicia of nonobviousness serve a particularly important role in a case, like this one, where there is a battle of scientific experts regarding the obviousness of the invention. In such a case, the objective indicia provide an unbiased indication regarding the credibility of that evidence.

Kinetic Concepts, Inc. v. Smith & Nephew, Inc., 2012 U.S. App. LEXIS 16904, *61 (Fed. Cir.

Aug. 13, 2012). The evidence strongly supports Plaintiffs' assertion that the cycle control results produced by the OTCLO regimen were unexpected. Weighed with the other evidence of record, this Court is persuaded that Defendants have failed to show, by clear and convincing evidence, that claims 1 and 4 of the '815 patent are invalid as obvious.

Defendants' principal obviousness argument could serve as a textbook example of an argument founded on hindsight. Defendants argue that the only difference between a regimen disclosed in the prior art '006 patent and the regimen disclosed in claims 1 and 4 of the '815 patent is a reduction in the EE dosage of 10 µg. The truth of this assertion is undisputed. From this starting point, though, Defendants argue that the skilled artisan would have found it obvious to make such a change. This appears persuasive only from the perspective of the rear-view mirror, and it perfectly exemplifies an obviousness argument which works backward from the invention. In hindsight, it is easy to compare the OTC regimen with the OTCLO regimen and see that, for sure, the only difference is 10 µg in the EE dosage. This key observation, however, is pure hindsight: it is only apparent after the fact of the invention of the OTCLO regimen.[11] Defendants' principal obviousness argument appears to start with the invention and work backwards. Defendants appear to have "simply retraced the path of the inventor with hindsight, discounted the number and complexity of the alternatives, and concluded that the invention . . . was obvious." Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 520 F.3d 1358, 1364 (Fed. Cir.

[11] The question of whether a skilled artisan would have seen a reason to reduce the EE dosage in the OTC regimen by 10 µg is itself a question that makes sense only from the perspective of hindsight: Defendants have pointed to no other significance to the number 10, but for the fact that, in hindsight, it is the difference in EE dosages. A key question that Defendants did not address is: why would the skilled artisan have wanted to reduce the EE dosage in the OTC regimen by 10 µg? Why not 8 µg, or 12 µg? The choice of 10 µg is pure hindsight.

2008).

The obviousness inquiry seeks to determine whether there is an obvious path that starts with the problem facing the skilled artisan at the time of invention, and ends with the invention at issue. As the Federal Circuit commented, discussing the Supreme Court's approach to the obviousness inquiry in KSR:

> The Supreme Court's analysis in *KSR* thus relies on several assumptions about the prior art landscape. First, *KSR* assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions. Second, *KSR* presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound.

Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd, 533 F.3d 1353, 1359 (Fed. Cir. 2008).[12] Thus, the starting point for the obviousness inquiry is the skilled artisan's identification of a problem. On this point, there is no dispute that the art was seeking oral contraceptive regimens with decreased estrogenergic side effects. For Defendants' argument to work, though, they must show how the skilled artisan, with this in mind, would have looked to the '006 patent for help in solving the problem. On this point, Defendants have offered nothing. There is no evidence of record that explains why a skilled artisan would have been motivated to modify the '006 patent, rather than some other prior art regimen. Thus, a vital step has been missed: defining the problem from within the perspective of the skilled artisan. It appears that Defendants "used the invention to define the problem that the invention solves." Mintz v. Dietz & Watson, Inc., 679 F.3d 1372,

[12] Similarly, in a pre-KSR case, the Federal Circuit held that "the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." In re Rouffet, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

1377 (Fed. Cir. 2012).

The instant case bears some similarity to the recent case of Kinetic Concepts. In Kinetic Concepts, the Federal Circuit first concisely stated the legal framework for the analysis that followed:

> While the Supreme Court made clear that a mechanical application of the teaching-suggestion-motivation test, requiring an explicit teaching in the prior art, is inappropriate, we must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention.

2012 U.S. App. LEXIS 16904 at *64 (citation omitted). The Federal Circuit then observed that the challenger "never offered evidence articulating why a person having ordinary skill in the art would combine the primary references to obtain the disclosed inventions." Id. at 64-65. Moreover, the evidence showed "significant evidence of teaching away." Id. at 67. The key inventive insight was that negative pressure healed wounds, and the Federal Circuit concluded:

> On the basis of this evidence, hindsight provides the only discernable reason to combine the prior art references. Unless one knew that negative pressure could be used to treat wounds, there would be no reason to combine the prior art to arrive at the claimed device and methods.

Id. This reasoning applies to the instant case. Defendants have not offered evidence explaining why the skilled artisan would begin to solve the problem by looking to modify the '006 patent. The evidence also shows significant evidence of teaching away from the claimed invention. The only discernable reason to think of modifying the '006 patent is hindsight since, unless one knew that reducing the EE dosage of the OTC regimen by 10 μg would result in equivalent cycle control, there would be no reason to do so.

C. Obviousness-type double patenting

The Federal Circuit has recently described the assertion that there is no difference between obviousness under § 103 and obviousness-type double patenting as "not entirely correct." Otsuka Pharm. Co. v. Sandoz, Inc., 678 F.3d 1280, 1297 (Fed. Cir. 2012). In Ostuka, the Court described the two inquiries as "analogous," but with important differences. Id. The Federal Circuit explained that, in a case involving a chemical compound patent, the two have a different focus. Id. Both inquiries "require[] identifying some reason that would have led a chemist to modify the earlier compound to make the later compound with a reasonable expectation of success." Id. The inquiries differ, however, in their focus. In a chemical compound case, the obviousness inquiry begins before the prior art patent, and asks both whether there was a reason why the artisan would have selected the compound in the first patent as the lead compound, and then whether there was a reason to modify it. Id. The obviousness-type double patenting inquiry, on the other hand, looks first to the earlier patent, and only asks whether there was a reason why the artisan would have modified it to create the later-patented invention. There is no suggestion from the Federal Circuit in Otsuka that these principles are not generally applicable to every kind of subject matter.

Applying these principles to the instant case, in the obviousness inquiry, this Court found, *inter alia*, that Defendants had failed to show a reason for the skilled artisan to choose the OTC regimen to modify. This finding is irrelevant to the inquiry into obviousness-type double patenting. For claim 1 of the '815 patent, this inquiry begins with claim 10 of the '554 patent; for claim 4 of the '815 patent, the inquiry begins with claim 9 of the '006 patent. These earlier patent claims claim the OTC regimen. The obviousness-type double patenting inquiry asks

whether it would be obvious to modify the OTC regimen to create the OTCLO regimen.

The Federal Circuit applies the following principles when considering a validity challenge based on obviousness-type double patenting:

> Obviousness-type double patenting is a judicially created doctrine that prohibits a party from obtaining an extension of the right to exclude through claims in a later patent that are not patentably distinct from claims in a commonly owned earlier patent. We have identified two steps in an obviousness-type double patenting analysis. First, a court construes the claim in the earlier patent and the claim in the later patent and determines the differences. Second, it determines whether those differences render the claims patentably distinct. A later patent claim is not patentably distinct from an earlier patent claim if the later claim is obvious over, or anticipated by, the earlier claim.

Pfizer, Inc. v. Teva Pharms. USA, Inc., 518 F.3d 1353, 1363 (Fed. Cir. 2008) (citations omitted).

The parties have disputed the role of secondary considerations evidence in this inquiry. After post-trial briefing was completed, the Federal Circuit decided Eli Lilly & Co. v. Teva Parenteral Meds., Inc., 2012 U.S. App. LEXIS 18029 (Fed. Cir. Aug. 24, 2012). As Plaintiffs observed, Lilly makes clear that evidence regarding secondary considerations is not barred from the obviousness-type double patenting inquiry:

> When offered, such evidence should be considered; a fact-finder "must withhold judgment on an obviousness challenge until it has considered all relevant evidence, including that relating to the objective considerations." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1079 (Fed. Cir. 2012).

Id. at *26. Furthermore, Lilly states clearly the difference between the inquiry into obviousness and the inquiry into obviousness-type double patenting:

> As a general rule, obviousness-type double patenting determinations turn on a comparison between a patentee's earlier and later claims, with the earlier patent's written description considered only to the extent necessary to construe its claims. . . . The focus of the obviousness-type double patenting doctrine thus rests on preventing a patentee from claiming an obvious variant of what it has previously

claimed, not what it has previously disclosed.

Id. at *19. Given that this Court has ruled that the patent at issue is not obvious, the present question is: does any difference in the law of obviousness-type double patenting lead to a different conclusion? As noted, Lilly has made clear that Defendants are incorrect in their assertion that secondary considerations are not part of this inquiry.

The question of whether it would have been obvious to the skilled artisan to modify the OTC regimen to create the OTCLO regimen has been discussed thoroughly *supra*. In short, while the skilled artisan might have thought to lower the estrogen dosage by 10 µg so as to reduce side effects, the evidence of teaching away in the art and of the unexpected results in terms of cycle control with the OTCLO regimen is significant, and this Court concludes that Defendants have not proven that it would have been obvious to the skilled artisan to reduce the EE dosage of the regimens disclosed in the prior art patents by 10 µg, creating the OTCLO regimen. This Court finds that Defendants have failed to prove, by clear and convincing evidence, that claims 1 and 4 of the '815 patent are invalid over claim 10 of the '554 patent or claim 9 of the '006 patent, under the doctrine of obviousness-type double patenting.

Pursuant to FED. R. CIV. P. 52(a), the Court presents its findings of fact and conclusions of law.

FINDINGS OF FACT

I. This Opinion incorporates by reference all stipulated facts set forth in the Final Pretrial Order.

II. Based on the evidence presented at trial, this Court now makes the following findings of fact:

1. The applicant filed the provisional patent application which ultimately led to the '815 patent on December 23, 1998. This is the critical date.
2. The genus of treatment regimens disclosed in the prior art '006 patent contains many millions of species.
3. The skilled artisan could not have at once envisaged each species within this genus.
4. The K90 study was a head-to-head study which found no statistically significant differences on cycle control measures between the OTC and OTCLO regimens.
5. There is no clinically meaningful difference in cycle control between the OTC and OTCLO regimens.
6. Although, as of the critical date, the trend in the art was toward oral contraceptive regimens with lower EE dosages, there was substantial uncertainty about whether low-EE regimens would provide comparable cycle control to higher-EE regimens.
7. A skilled artisan, as of the critical date, would have believed that cycle control was a function of both the estrogen and progestin dosages in an oral contraceptive regimen.
8. A skilled artisan, as of the critical date, would have expected that reducing the EE dosage of the OTC regimen from 35 µg to 25 µg would have produced some deterioration in cycle control.
9. A skilled artisan, as of the critical date, would have found the fact that there was no clinically meaningful difference in cycle control between the OTC and OTCLO regimens to be surprising and an unexpected result.

10. A skilled artisan, as of the critical date, would have believed that changing the OTC regimen by reducing the EE dosage would produce both positive and negative clinical effects. Among the positive effects was reduction in nuisance side effects. The chief negative effect was reduction in cycle control.

11. The Akerlund and Enrikat studies taught that reducing an existing OC regimen's EE dosage by 10 µg resulted in a deterioration in cycle control.

12. Defendants have not demonstrated a reason why a skilled artisan, as of the critical date, faced with the problem of reducing estrogen side effects from OC use, would have looked to the '006 patent to solve that problem.

13. Defendants have not demonstrated a reason why a skilled artisan, as of the critical date, faced with the problem of reducing estrogen side effects from OC use, and having decided to look to the '006 patent to solve that problem, would think to modify the OTC regimen to reduce the EE dosage by 10 µg.

14. Defendants have not demonstrated a reason why a skilled artisan, as of the critical date, who had decided to reduce the EE dosage of the OTC regimen, would have decided to reduce the EE dosage by precisely 10 µg.

15. As a pharmaceutical product on the market, the OTCLO regimen has achieved commercial success.

16. As a pharmaceutical product on the market, the OTCLO regimen has received industry praise.

CONCLUSIONS OF LAW

1. This Court has jurisdiction over this case pursuant to 28 U.S.C. § 1331.

2. The parties accept this Court's personal jurisdiction.

3. Venue is proper in this district pursuant to 28 U.S.C. § 1391(b).

4. Numerous prior art references taught away from the invention disclosed in claims 1 and 4 of the '815 patent. This teaching away appears in two areas: 1) references that taught that, generally, decreasing an OC regimen's estrogen dose produced deterioration in cycle control; and 2) more specifically, the Akerlund and Endrikat studies taught that reducing an existing OC regimen's EE dosage by 10 μg produced a substantial deterioration in cycle control.

5. Because of the prior art teaching away from reducing EE dosage below 30 μg, the skilled artisan in December 1998 the skilled artisan would not have had a reasonable expectation of success in modifying the OTC regimen to create the OTCLO regimen.

6. The fact that there was no clinically meaningful difference in cycle control between the OTC and OTCLO regimens was an unexpected result.

7. In this case, the secondary considerations evidence of unexpected results, commercial success, and industry praise is highly relevant to the finding of nonobviousness.

8. The '006 patent did not expressly spell out a definite and limited class of compounds that could enable a person of ordinary skill in the art to at once envisage each member of this class.

9. Defendants have not proven by clear and convincing evidence that claims 1 and 4 of the '815 patent are invalid as anticipated, pursuant to 35 U.S.C. § 102.

10. Defendants have not proven by clear and convincing evidence that claims 1 and 4 of the ’815 patent are invalid as obvious, pursuant to 35 U.S.C. § 103.

11. Defendants have not proven by clear and convincing evidence that claims 1 and 4 of the ’815 patent are invalid under the doctrine of non-statutory double patenting.

12. Claims 1 and 4 of U.S. Patent No. 6,214,815 are valid.

An appropriate Order follows.

s/ Stanley R. Chesler
Stanley R. Chesler, U.S.D.J.

Dated: September 11, 2012